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(54) Title: AQUEOUS INSECTICIDAL POUR-ON FORMULATION

(57) Abstract

A topically acceptable aqueous pour-on formulation adapted for localised external application to an animal, which format includes an effective amount of a water insoluble insect growth regulator (IGR), a suspending agent, a surfactant or mixture of surfactants, and an aqueous carrier

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Aqueous Insecticidal Pour-on Formulation

Field of the Invention

The present invention relates to an aqueous pour-on formulation of water insoluble insect growth regulator (IGR), and a method of treating animals using this formulation.

Background Art

Traditionally, animals have generally been treated for the control of parasites, by either dipping the whole animal in a bath containing a parasiticidally effective agent or by spraying the entire body surface of the animal with such an agent. More recently, it has been found that a number of parasiticidally effective substances may be applied by localised application (so-called "pour-on" application). Although the parasiticidally effective substance is supplied by localised application, the active agent migrates so as to protect the whole external surface of the animal. By "localised application" it is meant that the active ingredient is only applied to a minor portion of the outer surface of the animal, generally as a line or spot on the animal's back.

Prior Art Formulations

(a) Non Aqueous Pour-On Formulations

Various pour-on formulations are described in Australian patent nos. 560078, 563723, and 546672. In most pour-on formulations, and in all current water insoluble IGR pour-on formulations known to the inventors, the active agent is dissolved in a non-aqueous solvent system to produce a suitable pour-on formulation.

It has become apparent that non-aqueous pour-on formulations also possess a number of disadvantages. In particular, the formulation may pose handling problems caused by the flammability or toxicity of the solvents, and lead to high tissue residue levels in animals treated with the formulations.

Formulations based on water immiscible solvents would either run off wet animals or be washed off by rainfall which occurred after treatment.

On contact with water, the active rapidly precipitates out of non-aqueous formulations which are based on water miscible solvents. If this formulation is applied to a wet animal, or if the animal is exposed to rain before the treatment has dried on the animal, the active precipitates out of solution and is deposited along the back of the animal, the solvents also being washed away by the rain. This hinders or prevents the spread of the active ingredient around the entire animal. This phenomenon is particularly important to those areas on the underside of the animal. This reduces the effectiveness of solvent only based formulations under these conditions.

(b) Aqueous Dip Formulations

An aqueous dip formulation of IGR is also known. However, such a dip formulation would not be suitable as a pour-on formulation in either the undiluted or diluted state for the following reasons.

- Undiluted Dip Formulation

This would not be satisfactory because:

(i) In order to deliver the same amount of active per animal, the dose volume would be too small. That is, 2mL would be applied to the majority of animals, which would be a major issue for accurate dosing by farmers. A very small dose volume would be too localised to allow spreading to all parts of the animal as described above.

(ii) Due to the high levels of surfactants in an undiluted dip formulation, the presence of water, particularly high rainfall, would tend to wash the active off the animal.

- Diluted Dip Formulation

This situation would arise where the above-

mentioned dip formulation is diluted to achieve what would be considered a satisfactory concentration of active. However, this would not be satisfactory for the following reasons:

(i) If the dip formulation were diluted in a backpack or drum, the active would almost immediately commence to settle out of the formulation due to dilution of the suspending agent. This would create under/over dosing as described above.

(ii) Because the sedimented active would no longer be associated with the spreading/wetting agents, it would essentially be deposited along the line of application and have no means to disperse.

With regard to the possibility of aqueous pour-on formulations, and based on non-aqueous pour-on formulations, it would be expected by those skilled in this art that aqueous pour-on formulations containing water insoluble IGRs would not be effective because of problems with spreading and physical stability as follows.

- Spreading

It has generally been believed that a non-aqueous solvent is required to both dissolve the water insoluble IGR and help disperse the active so that it reaches all parasites on the animal. Without such spreading, the active would not reach all of the parasites, and would therefore be ineffective. Such spreading, in particular with sheep, also involves the movement of the active into the greasy layer of the wool. This is facilitated by the solvents which "push" the active into the layer while at the same time providing the physical spreading described above.

- Physical Stability

Because of the insolubility of the IGR in water, it is necessary to "suspend" the active in the formulation so that it does not settle on standing. If such settling

occurs to a significant degree, then it is difficult to redisperse it to achieve an accurate dose rate for application to the animal. Thus, there is in effect a caking of the active at the bottom of the container. This is a major reason why many aqueous suspensions have problems. The result is that an animal treated with product from the upper part of the container is underdosed, while an animal treated with the product from the lower part of the container is overdosed. This may have fatal consequences.

Aqueous formulations of water insoluble IGRs are more accurately described as suspensions. It would be expected that when such formulations are applied to animals as pour-ons, the suspended active would remain at the site of application, thereby exacerbating the spreading problems described above. Furthermore, it has been shown that when other water insoluble actives are applied to animals such as sheep in an aqueous pour-on formulation, the majority of the active grows out with the wool staple, effectively being carried away from the skin surface where it is needed to control the parasites.

Disclosure of the Invention

It has now been surprisingly found that an aqueous based pour-on formulation containing a water insoluble insect growth regulator(IGR) and a blend of surfactant and wetting agents is efficacious in controlling sheep lice. The formulation has the advantage over traditional non-aqueous solvent based formulations because it is rainfast and leads to very low pesticide tissue residue levels in the animals after application.

A surprising demonstration of the efficacy of this pour-on formulation is that at concentrations of 12.5 and 25.0 g/L diflubenzuron, when applied as a 20 ml dose along the backline of sheep, 100% lice kills were reported within 20 weeks. The majority of lice (95%) were killed within 10 weeks of application with the rest being killed over the

remainder of the 20 week period.

It has also surprisingly been found that adding the formulations of this invention to an already wet animal does not affect the efficacy of the formulation. Likewise, if it rains shortly after the formulations of this invention are applied, the speed of efficiency of the active is increased compared to situations where no rainfall occurs after treatment. In both instances, it is believed that the surfactants promote the spread of the active over the surface of the animal.

Thus, in a first aspect, the present invention provides a topically acceptable aqueous pour-on formulation adapted for localised external application to an animal, which formulation includes an effective amount of a water insoluble insect growth regulator (IGR), a suspending agent, a surfactant or mixture of surfactants, and an aqueous carrier.

Because of the insolubility of IGR in water, it is necessary to suspend the active in the formulation so it does not settle on standing. Accordingly, it is necessary to include in the formulation a sufficient amount of a suspending agent.

In a second aspect, the present invention provides a method for controlling external parasites on an animal which method includes externally applying to an animal an effective amount of a aqueous pour-on formulation adapted for localised external application to an animal, which formulation includes an effective amount of a water insoluble IGR, a suspending agent, a surfactant or mixture of surfactants, and an aqueous carrier.

Any water insoluble IGR could be used in the formulation according to the present invention. Suitable IGRs include diflubenzuron, triflumuron, fluazuron, and methoprene. A particularly preferred IGR is diflubenzuron. For the formulation to be effective, the IGR must be suspended in the aqueous carrier.

Suitable suspending agents include xanthan gum, colloidal silica, bentonite, polyvinyl pyrrolidone, cellulose derivatives and alginates. The particularly preferred suspending agent is xanthan gum.

Any anionic or nonionic surfactant could be used in this formulation. A preferred anionic surfactant is alkylated naphthalene sulphonate, formaldehyde polymer, sodium salt. An effective amount of surfactant must be incorporated into the formulation to provide sufficient dispersant activity when applied to the animal. Preferred non-ionic surfactants are alkyl polysaccharides; alkyl phenol ethoxylates. A preferred alkyl phenol ethoxylate is nonyl phenol ethoxylate.

Other ingredients may be suitably included, for example, wetting agents, thickeners, humectants, preservatives, buffers, anti-foaming agents, diluents, excipients, adjuvants, and/or carriers. Actives which have an immediate effect (ie "knock down"); dyes (scourable, water soluble); antioxidants or UV stabilizers (eg oxybenzone); and thixatropic agents may also be added. A preferred humectant is polyethylene glycol.

Thus, in a third aspect, the present invention provides a method for formulating a topically acceptable aqueous pour-on formulation adapted for localised external application to an animal, which method comprises forming a first component by mixing a humectant and non-ionic surfactant until homogenous; adding water and mixing until homogenous; adding buffer and anionic surfactant; adding insect growth regulator (IGR); forming a second component by mixing humectant and thickener; and combining said first and second components.

Suitably, the first and second components are diluted to a desired and final volume.

In addition, suitably, the IGR is milled to form a particle size of between about 2 to about 5 μm.

Suitable ranges for the ingredients are as follows:

a) Active	5 - 50g/L
b) Surfactants (non-ionic)	10 - 100g/L
c) Surfactants (anionic)	1 - 20g/L
d) Wetting Agent	1 - 20g/L
e) Thickener	3 - 10g/L

The "normal" ratio of the above would be a):b):c):d):e)=5:6:1:1:1. A more general description of the ratio would be active:surfactants/wetting agents/thickeners=1:2. These ratios would not be expected to vary significantly with type of active or surfactants. The most effective ratio is that of the most preferred formulation which has been "balanced" to optimise all of the above. The optimum pH for this formulation is in the range pH 5-9.

A particularly preferred formulation using the ranges of concentrations above would include diflubenzuron as the active; nonyl phenol ethoxylate, alkylated naphthalene sulfonate, formaldehyde polymer, sodium salt, as the mixture of surfactants; sodium lauryl sulfate as a wetting agent and Xanthan gum as a thickener or suspending agent.

Suitably, pour-on formulations include a colouring agent to enable the user to visually monitor the application of the formulation to the animal. The nature of the coloring agent is unimportant and a wide variety of suitable dyes and pigments will be known to the skilled person.

Suitably, the ingredients are formulated as follows: (a) half of the propylene glycol and non-ionic surfactant mixed in a mixing vessel until homogeneous. Water is then added and mixed until homogeneous. This is followed by buffer and anionic surfactant. Typically, anti-foam is then added and the mixture stirred. (b) The active ingredient is then added and mixed until homogeneous. (c) The second half of the propylene glycol is mixed with the Xanthan gum and then added and again, the mixture stirred

well until thorough mixing has occurred. The final volume is then adjusted with water if necessary.

The pour-on formulation may be formulated for application by a spray technique, for example, as an aerosol using a liquid or gas as propellent.

Depending on the efficacy of the particular active agent used, the formulation will generally contain from about 5 to about 50 g/L of the active agent.

The external parasites which may be treated in accordance with this invention include ticks, fleas, flies (for example, sheep blow fly, buffalo fly, nuisance fly), lice (for example, cattle and sheep lice) and mites (for example, sheep mites). The insects and parasites mentioned are indicative only, and numerous other insects and parasites can be treated by the method of the present invention. Suitably, the compositions and method of this invention may be used to treat the sheep body louse which is classified as follows: Order - *Phthiraptera*, Sub Order - *Mallophaga*, Family - *Trichodectidae*, Genus - *Damalinia* (Bovicola, Tricholdectes), Species - Bovicola ovis (Schrank).

The animal is preferably a mammal, and may be selected from sheep, cattle, deer, goats, pigs, dogs, and cats. The animal may also be a bird.

Best and Other Modes for Carrying Out the Invention

Preferred embodiments will now be described by way of non-limiting examples.

Example 1

Table 1 Diflubenzuron Sheep Lice Pour-on (25g/L)		
Component	Use	(g/L)
Diflubenzuron	Active Ingredient	25.00
Nonyl phenyl ethoxylate (eg. Teric GN15)	Non ionic	30.00
Alkylated naphthalene sulfonate, formaldehyde polymer, Sodium salt (eg. Morwet D425)	Anionic surfactant	3.00
Sodium lauryl sulphate BP (eg. Empicol LZVD)	Wetting agent	5.00
Xanthan Gum USP (eg. Keltrol F)	Thickener	5.10
Propylene Glycol USP	Humectant	60.00
1,2-Benzisothiazoline-3-one (20% w/w) in aqueous dipropylene gycol Solution (eg. Proxel GXL)	Preservative	1.00
Simethicone USP (eg. Antifoam A)	Antifoam	1.00
Citric Acid (Anhydrous BP)	Buffer	1.01 or qs
Disodium hydrogen phosphate-Anhydrous Food Grade	Buffer	13.30 or qs
Deionised Water	Diluent	qs to 1 L

Example 2

Details of Trial

Target pest

Order -*Phthiraptera*, Sub Order -*Mallophaga*, Family - *Trichodectidae*, Genus - *Damalinia* (Bovicola, Trichodectes), Species - *Bovicola ovis* (Schrank) and Common name - Sheep body louse.

Test animals

The sheep used in this study were a uniform line of Merino wethers heavily infected with lice.

The method requires examination of twenty partings each 10cm long, along two contours on the left and right sides covering the wool growing regions of the animal. At each of the 40 recorded sites all live adult lice are counted. Site counts are summed to give a total count for the animal.

Assessing lice populations in this manner also allows the production of a map, showing how the lice are distributed over the body of the tracer sheep.

Table 2 Treatment details				
Treatment	Active (mg) per sheep	Conc (g/L)	Sheep	Dose (mL)
Diflubenzuron	500	25.0	5	20
Diflubenzuron	250	12.5	5	20

Test treatments

Within 24 hours of shearing, treatments were applied as a single stripe along the backline of the sheep. The dose rate applied was based on 20mL of treatment per animal which is based on all test animals being in the 30.1 - 55kg weight range.

The delivery apparatus for each formulation was a commercial applicator, set to deliver 1 x 20mL doses to the sheep backline. The gun was calibrated using a volumetric cylinder and checked twice before and once after treatment.

To avoid the possibility of rain complicating the post treatment situation the sheep were kept in pens for a minimum of 48 hours. Then on the morning of the 25th day of the trial, they were placed into their paddocks.

Lice assessments were made on all sheep 2, 5, 10 and 20 weeks after treatment.

Example 3

Effect of diflubenzuron formulations on concentrations of sheep lice [group arithmetic lice counts (standard deviations)]

Table 3 Mean Lice Counts						
Diflubenzuron (g/L)	Weeks after treatment					
	0	2	5	10	15	20
25.0	120.6 (74.2)	17.2 (9.0)	4.4 (7.7)	1.4 (2.6)	1.0 (1.4)	0.0 (0.0)
12.5	161.8 (124.7)	6.8 (2.9)	1.8 (2.50)	0.4 (0.9)	0.0 (0.0)	0.0 (0.0)

Table 4 Field Efficacy (Control of sheep lice) Diflubenzuron Concentration is 25g/L

Trial No	Location	Animal used	Pre treatment mean lice count	% Lice reduction after:		
				6 weeks	12 weeks	20 weeks
1	Uralla, N.S.W.	1309 fine wool merinos	156	98.1	98.7	100
2	Guyra, N.S.W.	2000 super fine wool	41	100	100	100
3	Crookwell, N.S.W.	680 medium fine wool merinos	242	91.3	99.6	100
4	Lucindale, N.S.W	1094 strong wool merinos	35	99.8	100	100
5	Coonalpyn, S.A.	1101 strong wool merinos	142	99.6	100	100
6	Lismore, Vic	812 super fine merinos	51	99.5	100	100

Example 4

Efficacy Trial

Effect of diflubenzuron in 12.5 and 25.0 g/L pour-on formulations (corrected lice counts) [Results of Table 3 converted to % lice reduction]

Table 5

Diflubenzuron (g/L)	% Lice reduction after:				
	2 weeks	5 weeks	10 weeks	15 weeks	20 weeks
25.0	69.6	83.4	94.8	96.4	100.0
12.5	91.0	94.9	98.9	100.0	100.0

Example 5

Results of Wetting Trial

Table 6 Group mean lice counts

Group No	Treatment	Wetting	Days Post Treatment				
			0	22	44	84	142
1	25 g/L diflubenzuron	No wetting	92.0	2.5	0.5	0.3	0.2
2	25 g/L diflubenzuron	25mm rain before treatment	105.5	5.8	0.3	0.2	0.0
3	25 g/L diflubenzuron	25 mm rain after treatment	110.0	0.7	1.2	0.3	0.0
4	Untreated	25 mm rain before treatment	92.7	13.5	10.5	2.2	17.0
5	Untreated	No wetting	106.3	15.7	7.0	2.0	17.5

Table 7 Effect of rain on diflubenzuron pour-on (percent reductions)

Group No	Treatment	Wetting	Days Post Treatment			
			22	44	84	142
1	25 g/L diflubenzuron	No wetting	81.6	86.8	82.7	98.7
2	25 g/L diflubenzuron	25mm rain before treatment	62.8	95.7	89.9	100.0
3	25 g/L diflubenzuron	25 mm rain after treatment	95.7	83.6	85.6	100.0
4	Untreated	No wetting	1.4	-72.0	-26.1	-11.4

Note that these reductions have been calculated using the mean lice counts of Group 5, that is, the sheep kept dry. The following formula was used to calculate percent lice reductions.

% reduction = [1-(Untreated PT/Treated PT x Treated Time T/Untreated Time T)]1 X 100, where PT is average lice

number, and T is the average lice number at time post treatment.

Example 6

Pen efficacy trial (Control of cattle lice)

Efficacy of 25 g/L diflubenzuron pour-on against cattle lice.

Table 8

Group No	Dose Rate mg/kg	Pre treatment mean lice counts	% Lice reduction after:					
			14 days	28 days	42 days	60 days	72 days	84 days
1	5	99	57.7	52.5	94.8	92.2	95.7	87.9
2	10	89	68.7	62.9	96.2	99.3	98.1	100
3	15	97	81.9	62.7	94.6	95.1	99.0	100

Example 7

Field Efficacy (Prevention of strike by sheep blowfly)

Fourteen field efficacy trials were carried out under a range of climatic conditions throughout the eastern states of Australia. The data generated showed that the 25 g/L diflubenzuron formulation gave a high level of protection against body and crutch strike. Less than 0.1% of the 2316 sheep treated suffered body strike and 0.35% crutch strike. Fly pressure was measured using 2 flytraps within each paddock housing the treated sheep.

Example 8

Pen efficacy trials (Larval implant studies to demonstrate efficacy against strike by sheep blowfly, *Lucilia Cuprina*).

Pen studies have demonstrated that the aqueous product, when applied as a spray-on along the backline of long wooled sheep, is efficacious against the larval stages of the sheep blowfly, *Lucilia cuprina*.

Example 9

Tissue Residues

Tissue residue studies were carried out following application of the aqueous pour-on to both sheep and cattle. (Reference is made to page 1, lines 34 and 35 where it is mentioned that treatment with non aqueous pour-on formulations can lead to high tissue residues in animals treated with these formulations.)

Table 9

Sheep: Diflubenzuron residues after treating at a dose rate of 20 mg/kg

Note: Limit of quantitation (LOQ) = 0.02 mg/kg

	Level of diflubenzuron residues in tissues (mg/kg)				
Days post treatment	Muscle	Liver	Kidney	Peri-renal fat	Inguinal fat
1	<LOQ	<LOQ	<LOQ	0.03 max	0.02 max
3	<LOQ	<LOQ	<LOQ	0.02 max	0.04 max
7	<LOQ	<LOQ	<LOQ	0.02 max	0.03 max
14	<LOQ	<LOQ	<LOQ	<LOQ	0.02 max
21	<LOQ	<LOQ	<LOQ	<LOQ	0.05 max
42	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

Table 10

Cattle: Diflubenzuron residues after treating at a dose rate of 15 mg/kg

Note:

1. Limit of quantitation (LOQ) = 0.02 mg/kg
2. Muscle, liver and kidney tissues have not been tested as the diflubenzuron will preferentially go into the fat tissues.

	Level of diflubenzuron residues in fat tissues (mg/kg)	
Days post treatment	Peri-renal fat	Inguinal fat
1	0.17	<LOQ
3	0.09	<LOQ
7	<LOQ	<LOQ
14	<LOQ	<LOQ

Example 10

Comparative stability of formulations containing nominally 25 g/L diflubenzuron and 25g/L triflumuron.

Table 11
Stability of aqueous triflumuron pour-on after 6 weeks accelerated testing

Storage Temp.	Appearance	pH	Visosity Cps	Assay g/L
4°C	Purple suspension	7.59	922	24.0
30°C	Purple suspension	7.53	800	24.2
40°C	Purple suspension	7.48	772	23.6
50°C	Purple suspension	7.44	818	24.1

Table 12
Stability of aqueous diflubenzuron pour-on after 16 weeks accelerated testing

Storage Temp	Appearance	pH	Visosity Cps	Assay g/L
4°C	Purple suspension	7.56	835	25.1
30°	Purple suspension	7.48	821	25.3
40°C	Purple suspension	7.48	855	26.0
50°C	Purple suspension	7.50	913	26.0

Summary:

Efficacy data shows that rainfall pre or post treatment does not affect the efficacy of the formulation i.e. the product will be rainfast.

Insect growth regulators act by preventing the formulation of chitin during the insects moulting phase. They prevent the development of immature lice present in the fleece at the time of application and those which hatch from eggs in the following weeks. Adult lice die out naturally over a few weeks (can take up to 14).

The surprisingly quick knockdown effect (95.7% reduction in lice) of the formulation after post treatment rainfall (22 days) is shown. Four out of six sheep in the

group had no lice present. This demonstrates that the surfactants do help to spread the formulation when the product is applied in the wet.

The foregoing describes only some embodiments of the present invention and modifications obvious to those skilled in the art can be made thereto without departing from the scope of the invention.

Industrial Applicability

It should be clear that the present invention will find wide applicability in the agricultural and veterinary science areas.

CLAIMS

1. A topically acceptable aqueous pour-on formulation adapted for localised external application to an animal, which formulation includes and effective amount of a water insoluble insect growth regulator (IGR), a suspending agent, a surfactant or mixture of surfactants, and an aqueous carrier.

2. The formulation according to claim 1 wherein the IGR is diflubenzuron, triflumuron, fluazuron, or methoprene.

3. The formulation according to claim 2 wherein the IGR is diflubenzuron.

4. The formulation according to any one of claims 1 to 3 wherein the suspending agent is xanthan gum, colloidal silica, bentonite, polyvinyl pyrrolidone, cellulose derivatives or alginates.

5. The formulation according to claim 4 wherein the suspending agent is xanthan gum.

6. The formulation according to any one of claims 1 to 5 wherein the surfactant is an anionic or nonionic surfactant.

7. The formulation according to claim 6 wherein the anionic surfactant is an alkylated naphthalene sulphonate, formaldehyde polymer, sodium salt, and the non-ionic surfactant is an alkyl polysaccharide, or an alkyl phenol ethoxylate

8. The formulation according to any one of claims 1 to 7 further comprising wetting agents, thickeners, humectants, preservatives, buffers, anti-foaming agents, diluents, excipients, adjuvants, and/or carriers; actives which have an immediate effect; dyes; antioxidants and thixatropic agents.

9. The formulation according to claim 8 wherein the humectant is polyethylene glycol.

10. The formulation according to claim 8 or claim 9 wherein the IGR is about 5-50 g/L; the anionic surfactant is about 1-20 g/L; the non-ionic surfactant is about 10-100 g/L; the wetting agent is about 1-20 g/L and he thickener is about 3-10 g/L.

11. The formulation according to claim 10 wherein the IGR is diflubenzuron; the surfactants comprise nonyl phenol

ethoxylate, and alkylated naphthalene sulfonate, formaldehyde polymer, sodium salt; the wetting agent is sodium lauryl sulfate; and the thickener or suspending agent is Xanthan gum.

12. A method for controlling external parasites which method includes externally applying to an animal an effective amount of a aqueous pour-on formulation adapted for localised external application to an animal, which formulation comprises an effective amount of a water insoluble insect growth regulator (IGR), a suspending agent, a surfactant or mixture of surfactants, and an aqueous carrier.

13. The method according to claim 12 wherein the IGR is diflubenzuron, triflumuron, fluazuron, or methoprene.

14. The method according to claim 13 wherein the IGR is diflubenzuron.

15. The method according to claim 14 wherein the formulation further comprises a colouring agent.

16. The method according to any one of claims 12 to 15 wherein the formulation is applied as a spray technique.

17. The method according to claim 16 formulated as an aerosol using a liquid or gas as propellent.

18. The method according to any one of claims 12 to 17 wherein the IGR is from about 5 to about 50 g/L.

19. The method according to any one of claims 12 to 18 wherein the parasites include ticks, fleas, flies, lice and mites.

20. The method according to claim 19 wherein the flies may be sheep blow fly, buffalo fly or nuisance fly; the lice may be cattle or sheep lice; and the mites are sheep mites.

21. A method for formulating a topically acceptable aqueous pour-on formulation adapted for localised external application to an animal, which method comprises forming a first component by mixing a humectant and non-ionic surfactant until homogenous; adding water and mixing until homogenous; adding buffer and anionic surfactant; adding insect growth regulator (IGR); forming a second component by mixing humectant and thickener; and combining said first and second components.

22. The method according to claim 21 wherein the combined first and second components are diluted to a desired final volume.

23. The method according to claim 21 or claim 22 wherein the IGR is milled to form a particle size of between about 2 to about 5 μm.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 98/01046

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl[6]: A61K 9/10, 9/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC: A61K 9/10, 9/12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
AU: IPC as above.

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPAT: [DIFLUBENZURON: OR TRIFLUMURON: OR METHOPRENE] AND [XANTHUM GUM OR SILICA OR BENTONITE OR PVP OR POLYVINYLPYRROLIDONE OR CELLULOSE OR ALGINATE:] AND [SURF:] AND [INSECT: OR POUR:]
CAPLUS: [DIFLUBENZURON OR TRIFLUMURON OR FLUAZUROM OR METHODPRENE] AND [SURFACTANT] AND [INSECT OR POUR] AND [XANTHUM GUM OR SILICA OR BENTONITE OR PVP OR POLYVINYL PYRROLIDONE OR CELLULOSE OR ALGINATE]

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Derwent Abstract Accession No. 95-363517/47, Class A97 C03, JP 07247207 A (TAMURA SEIYAKU KK) 26 September 1995.	1-4, 6, 8-10, 12-23
X	Derwent Abstract Accession No. 93-392541/49, Class A97 C07 (C03) JP 05294801 A (ARITSUNE YAKUHIN KOGYO KK) 9 November 1993.	1-4, 6, 8-10, 12-23
A	US 5612047 (Duffy et al) 18 March 1997 Whole document.	1-23

☐ Further documents are listed in the continuation of Box C

☐ See patent family annex

* Special categories of cited documents:

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
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